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Solid-State Mid-Infrared Laser Facilitated Coronary Angioplasty: Clinical and Quantitative Coronary Angiographic Results in 112 Patients

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Background and Objective: **Holmium:YAG is a solid-state, investigational coronary laser device. Preliminary reports indicate the clinical potential for this laser; however, its safety and efficacy in a single center experience have not yet been reported and analyzed in detail.**
Study Design, Patients, and Methods: **One hundred and twelve consecutive symptomatic patients underwent percutaneous holmium:YAG laser (2.1 micron wavelength, 250–600 mJ/pulse, 5 Hz) facilitated coronary angioplasty. Sixty-six patients (Gr 1) had 74 thrombotic lesions, and 46 patients (Gr 2) had 55 thrombus-free stenoses.**
Results: **Overall laser success was achieved in 120 out of 129 lesions (93%), with 95% subsequent balloon angioplasty success. Laser and clinical successes among the two groups were similar. By quantitative coronary angiography, reduction in the percent diameter stenosis (mean ± SD) was similar (79 ± 16% to 37 ± 14% vs. 73 ± 16% to 37 ± 11.5%; P = NS) in both groups. However, minimal luminal diameter improved significantly more in Gr 1 patients, (0.7 ± 0.5 mm to 2.0 ± 0.5 mm, vs. 0.9 ± 0.4 mm to 1.8 ± 0.4 mm, $P = 0.03$). Angiographic and clinical complications were similar in patients with thrombus and without thrombus. No death, perforation, or Q-wave infarction occurred in the catheterization laboratory in either group. In-hospital mortality occurred in two patients from cardiac causes unrelated to the laser application. Of the 98 patients who reached the 6 month anniversary, 76 (77%) remained asymptomatic. The restenosis rate among the patients who underwent repeat angiography was 50%.**
Conclusions: **Solid-state, mid-infrared laser can be safely and successfully applied to symptomatic patients with thrombotic and nonthrombotic lesions. Similar to other debulking devices, the effectiveness of this laser in yielding long-term patency has not been proved.**

Key words: angioplasty, coronary, holmium, infarction, laser, thrombus

INTRODUCTION

The presence of coronary thrombus in the setting of unstable coronary syndromes and acute myocardial infarction has been well documented [1]. When present, thrombus is associated with an increased risk of complications during coronary balloon angioplasty [2]. Recent reports [3–6] sug-

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gest that solid-state, pulsed-wave, mid-infrared holmium:YAG laser angioplasty is feasible as a percutaneous coronary procedure for treatment of lesions considered not ideal for balloon angioplasty. However, the safety and efficacy of this technology in lesions containing thrombus have not been reported. The purpose of this investigation was twofold: (1) to assess the clinical and quantitative angiographic results in a series of 112 patients treated with percutaneous holmium: YAG (2.1 micron) laser-facilitated coronary angioplasty and (2) to determine the effect of this wavelength on intracoronary thrombus at the site of the target lesion.

METHODS

Study Patients

Between October 9, 1991 and August 15, 1993, percutaneous coronary holmium:YAG laser-assisted angioplasty was attempted in 112 patients with a total of 129 coronary artery stenoses (Table 1). Patients considered for this procedure were those with symptomatic coronary artery disease and objective evidence of myocardial ischemia sufficient to warrant balloon angioplasty or coronary artery bypass surgery, and angiographically documented stenoses of native coronary arteries or bypass grafts thought to be traversable with angioplasty guidewires. The majority of patients were referred for laser angioplasty, because they were not considered ideal candidates for balloon angioplasty due to lesion morphology or location, a previous unsuccessful attempt of balloon angioplasty, and/or multiple recurrences after balloon angioplasty [7]. Patients with an evolving myocardial infarction who did not qualify to receive thrombolytics, or received lytic agents but clinically failed to respond and underwent emergency coronary arteriography within 24 hours from the onset of chest pain, were considered for entry into the protocol if the infarct-related artery contained a large thrombus and/or a complex-type lesion [4]. This study is part of a nonrandomized multicenter trial. Informed consent was obtained under a protocol approved by the Food and Drug Administration and the Institutional Review Board at St. Paul-Ramsey Medical Center. These cases were comprised of a group representing 26% of the total number of balloon angioplasty procedures performed during this period.

Angioplasty Protocol

Pretreatment medication consisted of oral aspirin (325 mg) and a calcium channel antagonist administered the night before and the day of the procedure. Conventional 8 French or 9 French guiding catheters were used. A standard angioplasty regimen of heparin (10,000 U intravenous bolus injection), an intravenous nitroglycerin drip (adjusted to systolic blood pressure), and intracoronary nitroglycerin (100 μg) were given before baseline quantitative coronary cineangiography was performed.

Laser Equipment

A holmium:YAG (2.1 micron), solid-state, pulsed-wave laser generator (Eclipse 2100, Eclipse Surgical Technologies, Palo Alto, CA) was used. Laser output from the generator was activated with a foot pedal, delivering pulses of 250 microseconds, a pulse energy of 250–600 mJ/pulse, at a frequency of 5 Hz. If needed, the fluence of this device (1,750 mJ/mm^2 at a pulse energy of 350 mJ/pulse) can quickly be adjusted higher or lower without removal of the catheter from the coronary artery. Five sizes of multifiber laser catheters are available: (1) 1.2 mm, built of 27 optic fibers, 75 microns each, arranged concentrically around a central lumen for passage over a guidewire. This catheter has a fiber/catheter tip area ratio of 0.32 (minus guidewire lumen). (2) 1.4 mm, which consists of 40 optic fibers, 50 microns each, with a fiber/catheter tip area ratio of 0.095. (3) 1.5 mm, with 26 optic fibers, 100 microns each, and a fiber/catheter tip area ratio of 0.196. (4) 1.7 mm, with 49 optic fibers, 50 microns each, and a fiber/catheter tip area of 0.076. (5) 2.0 mm, with of 12 optic fibers, 100 microns each, and a fiber/catheter tip area of 0.92.

Laser Procedure

A 0.014 or 0.018 inch (0.036 or 0.046 cm, respectively) guidewire was separately advanced across the lesion into the distal coronary artery, with its position confirmed fluoroscopically. After extending the guidewire or utilizing a long 300 cm guidewire, a laser catheter was advanced over the guidewire up to the target lesion. Small injections of contrast medium (3 ml) confirmed the position of the laser catheter to be in direct contact with the origin of the lesion. The common, traditional lasing technique, which includes continuous delivery of pulses while slowly advancing the catheter along the target lesion, was utilized in the first 12 cases. However, in the following 100 cases, a "pulse and retreat" lasing technique was applied [8]. With this technique the operator delivers only a small number of pulses, typically

8–12, and then retracts the laser catheter back into the guiding catheter to permit unimpeded forward coronary blood flow. A 45–60 second pause is taken prior to the next lasing session to allow coronary relaxation. Contrast is injected for observation of the lasing site, and administration of intracoronary nitroglycerin is commonly used, taking into account the systolic blood pressure and other clinical, hemodynamic, and electrocardiographic parameters. A combination of tactile feedback and angiography is used to decide how many passes through the lesion are necessary. Once a laser catheter passes smoothly through the length of the lesion, no further passes are attempted. After laser application, balloon angioplasty was performed in all patients to maximally reduce the luminal stenosis. After overnight heparinization, all vascular sheaths were removed. Discharge medications included aspirin (325 mg/day) and other cardiac agents, as indicated.

Qualitative and Quantitative Coronary Arteriography

Cine angiograms of all patients were reviewed by the investigators for determination of lesion severity and complexity, and for identification of thrombus within the target lesion before and after laser treatment, and following adjunct balloon angioplasty. Using a valid method previously described [9], quantitative analysis of coronary stenoses before and after laser angioplasty, as well as after balloon angioplasty, was performed at an independent core laboratory at Stanford University (Palo Alto, California), which was blind to the clinical data and outcome of the procedure.

Procedure Definitions

Lesion complexity was graded according to the classification of the ACC/AHA Task Force [7], as modified by Ellis et al. [2] to include types B1 and B2, depending on whether one or more complex features were present. Multivessel disease was defined according to the definitions of the Coronary Artery Surgery Study [10]. Lesion length was measured with calipers, using catheter calibration to account for magnification, and was defined as the distance from the proximal to the distal shoulder spanning >50% stenosis in a nonforeshortened projection.

Laser success was defined according to the National Heart, Lung and Blood Institute (NHLBI) criteria [11] as passage of the laser catheter through the stenosis and a more than 20% reduction in the absolute minimal diameter stenosis. Procedural success was defined as final diameter stenosis of 50% or less after adjunct balloon angioplasty and the absence of a major complication (death, Q-wave or non–Q-wave myocardial infarction, or need for coronary artery bypass surgery) at any time during hospitalization.

Acute closure was defined according to Cook et al. [12], with corresponding Thrombolysis in Myocardial infarction (TIMI) grade 0–1 flow [13]. Coronary artery dissection [14,15] and perforation [16] were defined according to established criteria in the literature. Thrombus was defined as the presence of a globular or elongated filling defect surrounded by contrast medium, and usually located immediately downstream from a stenosis, or an area of contrast staining noted within the stenosis scheduled to be dilated [17]. Angiographic restenosis was defined as >50% diameter stenosis at the treated site, or by the need for revascularization (repeat angioplasty or coronary artery bypass surgery). Clinical restenosis was defined as angiographic restenosis or recurrence of angina, positive exercise treadmill test, or development of myocardial infarction related to restenosis of the lased artery. The overall restenosis rate was calculated by combining the angiographic and clinical restenosis rates in patients who did not undergo follow-up angiography.

Data Collection

During hospitalization, clinical, laboratory, and angiographic information were recorded and entered into a computerized data bank. Recorded data included age, sex, past medical history, Canadian Cardiovascular Society functional classification, location of treated vessel, preprocedural and postprocedural percent diameter stenoses, laser catheter size, laser energy output, number of laser pulses emitted, use of adjunctive balloon angioplasty, balloon size, and all complications. Clinical complications recorded included death, coronary artery bypass surgery, myocardial infarction, cerebrovascular accident, hematoma, and need for blood transfusion. Angiographic complications recorded included acute closure, perforation, dissection, thrombosis, spasm, and distal embolization. All patients were requested to return, even if asymptomatic, for follow-up angiography, which was performed at 6 months, or earlier in the presence of recurrent symptoms.

Statistical Analysis

Statistical analyses were performed using a standard statistical package (SPSS for OS/2 Release 4.1, Chicago, Illinois). Chi-square analyses were used to compare categorical variables. Three observation points were compared (prelaser stenosis, postlaser stenosis, and post–balloon angioplasty residual stenosis). For all three variables (visual estimates of percent stenosis, quantitative angiography for percent diameter stenosis and quantitative angiography for minimal luminal diameter), the one-way repeated measures analysis of variance (MANOVA) procedure was significant at $P < .001$. Since all multivariate repeated measure analyses were highly statistically significant, a series of paired t-tests was performed comparing all three observation points for all three variables. All data are presented as the mean ± SD.

TABLE 1. Clinical and Angiographic Findings in 112 Patients

Clinical findings	
Age (yr)	
Mean	59 ± 12
Range	38–90
Gender	
Male	77%
Female	23%
Angina	
Stable	21%
Unstable	58%
Acute MI	21%
Functional class (CCS)	
I	10%
II	16%
III	34%
IV	40%
Angiographic finding (129 stenoses)	
Vessel treated	
LAD	51%
LCx	14%
RCA	32%
SVG	3%
Repeat angioplasty	22%
Multivessel angioplasty	8%
Severity (%) stenosis before treatment (mean ± SE)	
QCA	77 ± 16
VE	94 ± 6

CSS, Canadian Cardiovascular Society; LAD, left anterior descending artery; LCx, left circumflex artery; QCA, quantitative coronary arteriography; RCA, right coronary artery; SVG, saphenous vein graft; VE, visual estimation.

RESULTS

Patients

Clinical characteristics and angiographic findings of 112 patients undergoing holmium: YAG laser-assisted coronary angioplasty at our institution are shown in Table 1. Seventy-seven patients were men and the mean patient age was 59 ± 11 years. Twenty-two percent of the patients underwent one or more prior balloon angioplasties of the lesion that received laser angioplasty. Eight percent of the patients had laser angioplasty as a part of multivessel angioplasty procedure.

Of the 24 patients with complicated acute myocardial infarction who are included in this series, 15 (63%) failed treatment with thrombolytics, 8 (33%) arrived to the medical center too late for thrombolytic administration, and 1 (4%) had contraindication to these agents. Clinically, each of these patients had continuous chest pain and ischemia that necessitated emergency coronary arteriography and revascularization. Thirteen (54%) of these patients had inferior wall infarction, seven (29%) had anterior wall infarction, and four (17%) presented with lateral infarction. Eight (33%) patients were in cardiogenic shock, 10 (42%) in Killip class III, and 6 (25%) in Killip classes I–II. TIMI flow prior to intervention was 1.2 ± 1.2 (mean ± SD).

Lesions

The 112 patients had a total of 129 stenoses treated with holmium laser. Lesions involved were as follows: 51% in the left anterior descending artery, 32% in the right coronary artery, 14% in the circumflex artery, and 3% in the saphenous vein graft. Sixty-six patients exhibited 74 thrombotic lesions, and 46 patients had 55 thrombus-free lesions. According to the AHA/ACC classification of lesion severity [5], 3% of the lesions were characterized as simple lesions (type A), whereas 79% were moderately complex (type B) and 18% were complex (type C).

Angiographic Characteristics—Influence of Thrombus

Of the 112 patients treated with holmium laser, 66 (Gr 1) had angiographic evidence of intracoronary thrombus and 46 had lesions without thrombus (Gr 2) (Table 2). There were no significant differences in age, gender, tobacco use, diabetes mellitus, or history of previous myocardial infarction angina class between the two groups. Patients with thrombus had significantly more multivessel disease than patients without intra-

TABLE 2. Clinical Characteristics in 112 Patients*

	Thrombus (Gr 1) (n = 66)	No thrombus (Gr 2) (n = 46)	*P* value
Age (yr)	59 ± 11.9	60 ± 11.8	0.660 (NS)
Male	56 (84.8)	30 (65.2)	0.202 (NS)
Previous CABGS	4 (6.1)	6 (13.0)	<0.01
Previous PTCA	8 (12.1)	17 (37.0)	<0.001
Multivessel disease	28 (42.4)	11 (23.9)	0.043
Previous MI	18 (27.3)	17 (37.0)	0.277 (NS)
Angina class			0.248 (NS)
I	7 (10.6)	4 (8.7)	
II	8 (12.1)	10 (21.7)	
III	20 (30.3)	18 (39.1)	
IV	31 (47.0)	14 (30.4)	

*Data are expressed as number (%) of patients. CABGS, coronary artery bypass graft surgery; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty.

TABLE 3. Characteristics of 129 Treated Lesions*

	Thrombus (n = 74)	No thrombus (n = 55)	*P* value
Vessel location			0.816 (NS)
SVG	2 (2.7)	2 (3.6)	
LAD	36 (48.7)	30 (54.6)	
RCA	26 (35.1)	15 (27.3)	
LCx	10 (13.5)	8 (14.6)	
Lesion type			0.0007
A	0 (0)	3 (5.5)	
B1	5 (6.8)	17 (30.9)	
B2	55 (74.3)	26 (47.3)	
C	14 (18.9)	9 (16.4)	
Length (mm)	15.4 ± 6.7	14.7 ± 7.7	0.630 (NS)
Ostial	3 (4.1)	5 (9.3)	0.329 (NS)
Eccentricity	47 (72.3)	26 (48.2)	0.002
Calcified	8 (10.8)	14 (25.5)	0.028
Total occlusion	17 (23.0)	3 (5.5)	0.006
Bifurcation	1 (1.4)	3 (5.7)	0.410 (NS)
Adjunctive balloon	72 (97.3)	54 (98.2)	0.74 (NS)
Stenosis severity			
VE	95.9 ± 4.5	92.8 ± 6.5	0.003
QCA: %Stenosis	79.2 ± 16.1	73.3 ± 15.9	0.052
MLD (mm)	0.7 ± 0.5	0.9 ± 0.4	0.026
Energy (watts)	2.5 ± 0.4	2.5 ± 0.4	0.707 (NS)

*Data are expressed as mean ± SD or the number (%) of lesions. VE, visual estimates; MLD, minimal luminal diameter; QCA, quantative coronary angiography. See Table 1 for the rest of the abbreviations.

coronary thrombus. Previous bypass surgery and previous balloon angioplasty were more prevalent in patients without thrombus than in those with this angiographic finding, reflecting the low incidence of saphenous vein grafts treated in this series and the high incidence of restenosis lesions without a thrombus. Most patients with thrombus had complex lesions (Table 3). As expected, lesions containing thrombus were more severely stenosed ($P = 0.003$).

No difference was found in lesion length and location (ostial, bifurcation) between stenoses with thrombus and stenoses without thrombus. Lesions containing thrombus were more often eccentric ($P = 0.002$) and calcified ($P = 0.028$) than those without thrombus. Total occlusions included 23% of the lesions with thrombus vs. 5.5% of the lesions without thrombus ($P = 0.006$). Adjunctive balloon angioplasty was performed in 97% of the lesions in patients with thrombus and in 98% of the lesions in patients without thrombus ($P = 0.74$). Coronary thrombus did not decrease the likelihood of clinical success (Table 4). Clinical success was achieved in 71 (95%) of 74 thrombus-containing lesions vs. 51 (93%) of 55 thrombus-free lesions ($P = 0.425$).

Quantitative Versus Visual Estimates of Coronary Stenosis

One hundred and five cine films were technically adequate for quantitative analysis. By quantitative angiographic analysis, the minimal luminal diameter increased from 0.8 ± 0.5 mm (mean ± SD) to 1.3 ± 0.5 mm after laser ablation ($P < 0.001$) and to 1.9 ± 0.5 mm following adjunct balloon angioplasty ($P < 0.001$) (Fig. 2). The mean percent diameter stenosis reduced from 77 ± 16% (mean ± SD) to 56 ± 14% after laser treatment ($P < 0.001$) and was further decreased by balloon angioplasty to 37 ± 13% ($P < 0.001$). By visual estimation, stenosis severity was reduced by laser from 94 ± 6% to 58 ± 19% ($P < 0.001$) and to 21 ± 15% following adjunct balloon angioplasty ($P < 0.001$).

TABLE 4. Procedural Success and Angiographic Results in 129 Lesions*

	Thrombus (n = 74)	No thrombus (n = 55)	*P* value
Clinical success	71 (95.9)	51 (92.7)	0.425 (NS)
Postprocedural stenosis			
VE	19.0 ± 17.9%	24.9 ± 21.5%	0.130 (NS)
QCA:			
% Stenosis	36.9 ± 13.8%	36.6 ± 11.5%	0.920 (NS)
MLD	2.0 ± 0.5	1.8 ± 0.4	0.03

*Data are expressed as the number (%) of lesions.
VE, visual estimation; QCA, quantitive coronary arteriography; MLD, minimal luminal diameter in millimeters.

By quantitative angiography, the severity of stenosis improved from 79 ± 16% to 37 ± 14% in patients with intracoronary thrombus compared with an improvement of 73 ± 16% to 37 ± 11.5% in patients without a thrombus (P = 0.920). By visual estimation, the severity of the stenosis was improved from 96 ± 4.5% to 19 ± 17% in patients with intracoronary thrombus compared with an improvement of 93 ± 6.5% to 25 ± 21.4% in patients without thrombus (P = 0.130). By quantitative angiography, minimal luminal diameter improved from 0.7 ± 0.5 mm (mean ± SD) to 1.3 ± 0.5 mm ($P < 0.001$) by laser and to 2.0 ± 0.5 mm by balloon ($P < 0.001$) in patients with intracoronary thrombus. In those without angiographic evidence of thrombus, it improved from 0.9 ± 0.4 mm (mean ± SD) to 1.2 ± 0.4 mm ($P <$ 0.002) and to 1.8 ± 0.4 mm by adjunct balloon angioplasty ($P < 0.001$). The patients with thrombus-containing lesions had more severe lesions (P = 0.026), but there was no significant difference between these two groups comparing the improvement in luminal diameter by laser (P = 0.11). The final results (Table 4) post–balloon angioplasty showed improved minimal luminal diameter among patients with intracoronary thrombus as opposed to those without thrombus (P = 0.03).

Procedural and Clinical Outcomes

Figure 1 depicts the results of this study. No mortality occurred in the cardiac catheterization laboratory during the procedure. The holmium laser catheter was able to traverse the target lesion and to reduce the percent diameter stenosis by ≥20% in 120 (93%) out of the 129 coronary artery stenoses. The average lesion length was 15.1 ± 7.1 mm. In three patients, each with a complex lesion, it was not possible to completely cross the target stenosis with a laser catheter because of vessel tortuosities proximal to the lesion, negating adequate guiding catheter support. In 109 patients the laser angioplasty was completed with application of 96 ± 75 pulses (mean ± SD) per patient. A 1.2 mm catheter was applied to 4% of the lesions, a 1.4 mm catheter was used in 36% of the lesions, a 1.5 mm catheter was applied to 40% of the lesions, a 1.7 mm catheter was used in 15% of the lesions, and a 2.0 mm catheter was utilized in 10% of the stenoses (in three patients more than one laser catheter size was used). Clinical success was achieved in 23 (96%) of the 24 patients with acute myocardial infarction (Fig. 3). TIMI flow increased from 1.2 ± 1.2 (mean ± SD) to 2.8 ± 0.7. Twenty-three of the 24 patients were discharged from the hospital. Figures 4 and 5 depict results in two patients.

Complications

Of the 112 patients, 2 (both with thrombus-containing lesions) died in the hospital from cardiac causes; however, these were not related to the laser application. One patient required emergency coronary bypass surgery for a significant dissection caused by adjunct balloon dilatation of the left anterior descending artery and was subsequently discharged. Seven patients (6%) had post–adjunct balloon dilatation, angiographic evidence of a stable linear dissection that neither impaired flow nor caused ischemia. Two patients (1.7%) had post laser a small, stable dissection without sequelae. No perforation occurred during laser angioplasty nor during adjunct balloon angioplasty nor adjunct directional atherectomy. Abrupt closure of the lased artery occurred in two patients in the cardiac catheterization laboratory, and in another patient 4 days following the procedure. All three were successfully treated with repeat balloon angioplasty.

Two patients sustained a non–Q-wave myocardial infarction (based on a pathologic rise in cardiac enzymes, but without symptoms) following the procedure. No patient developed a Q-wave infarction. There was no laser-related local thrombosis or side branch occlusion. Two patients had distal embolization. While spasm occurred in 5 of the first 12 patients (using the traditional lasing technique), it occurred in only one of the subsequent 100 patients (applying the "pulse and retreat" lasing technique) [8]. In each case, spasm responded to intracoronary injections of nitroglycerin or to balloon dilatation. Table 5 contains a comparison of the complications in both groups. The occurrence of embolization, myocardial infarction, abrupt closure, spasm, emergency CABGS, and dissections were not significantly different between the two groups.

Follow-Up

All patients were seen by the investigators in a follow-up clinic at 4 weeks and again at 2, 3, and 6 months to assess clinical status and clinical events [death, myocardial infarction, or any revascularization procedure (bypass surgery or coronary angioplasty)]. Six patients died within the 6 month follow-up period. Two patients were referred during the 6 month follow-up for elective bypass surgery for progressive disease of the non-

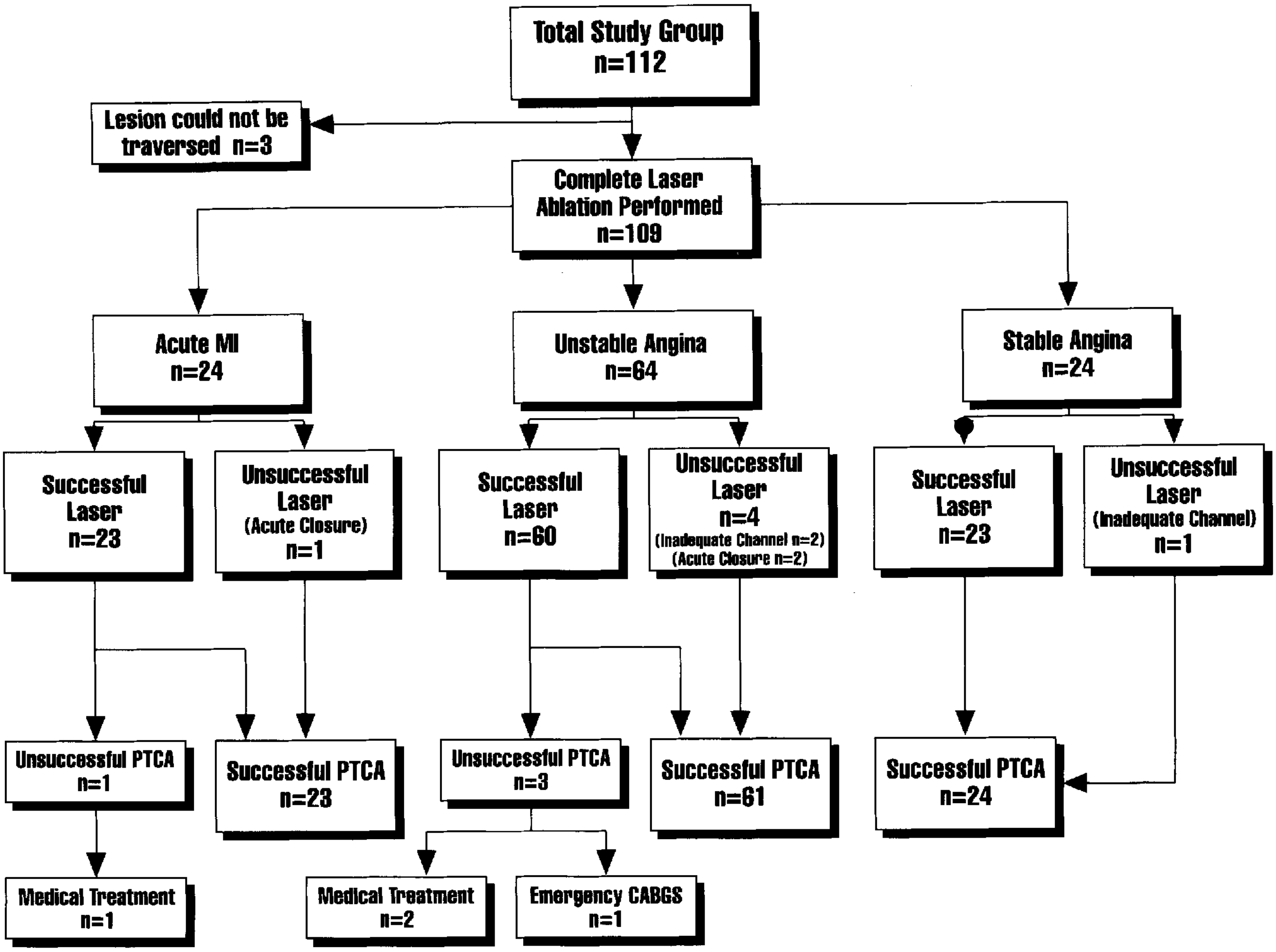


Fig. 1. Diagram of laser angioplasty results in 112 patients.

TABLE 5. Procedure Related Complications in 112 Patients*

	Thrombus (n = 66)	No thrombus (n = 46)	*P* value
Embolization	2 (3.0)	0 (0)	0.439 (NS)
MI			
Q-wave	0 (0)	0 (0)	—
Non–Q-wave	2 (3.0)	0 (0)	0.439 (NS)
Abrupt closure	3 (4.5)	0 (0)	0.338 (NS)
Spasm	3 (4.5)	3 (6.5)	0.648 (NS)
Emergency CABGS	1 (1.5)	0 (0)	0.589 (NS)
Major dissection	1 (1.5)	0 (0)	0.589 (NS)
Minor dissection	6 (9.1)	2 (4.4)	0.338 (NS)
Perforation	0 (0)	0 (0)	—
Death	0 (0)	0 (0)	—

*Data are expressed as the number (%) of patients.
CABGS, coronary artery bypass graft surgery; MI, myocardial infarction

lased coronary vessels. Both survived surgery and are asymptomatic.

Ninety-eight patients reached the 6 month anniversary after successful holmium laser angioplasty. Seventy-six (77%) of the 98 patients remained asymptomatic. Symptoms recurred in 22 (23%) patients. Angiographic restenosis was found in 19 (50%) out of 38 lesions originally treated. Of 57 asymptomatic patients who did not receive a repeat angiogram, 39 underwent exercise thallium testing or exercise echocardiography without chest pain and without evidence of ischemia, and two patients had evidence of ischemia but were treated medically. Five patients physically unable to exercise were clinically asymptomatic at the 6 month follow-up. Eleven patients refused any postprocedural evaluation, but they, too, are asymptomatic.

DISCUSSION

The major observations from this study are as follows: (1) Solid-state, mid-infrared laser assisted balloon angioplasty is safe and effective in

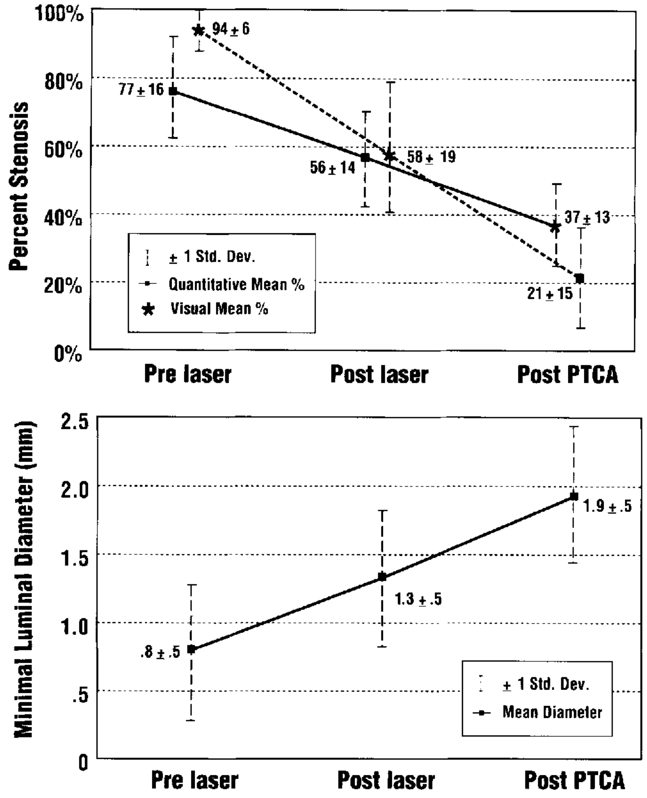


Fig. 2. Quantitative arteriographic analysis of percent luminal diameter vs. visual estimation (**top**), and minimal luminal diameter (mm) (**bottom**) before (pre) and after (post) laser angioplasty (laser) and balloon angioplasty (PTCA) in the 112 study patients. Data are presented as mean ± SD.

revascularization of symptomatic patients with lesions considered non-ideal for balloon angioplasty, achieving a high procedural success rate. (2) The immediate success of revascularization by this laser is not adversely influenced by the presence of intracoronary thrombus, an important marker of acute ischemic events, that is, unstable angina and myocardial infarction. (3) It is possible that the "pulse and retreat" lasing technique is accountable for a remarkably low complication rate, especially in thrombotic lesions.

Rational for Laser Assisted Coronary Angioplasty

Laser interventions have recently been introduced to overcome the limitations of conventional balloon angioplasty in the treatment of coronary artery disease [18]. The potential for excimer lasers to improve recanalization in lesions non-ideal for balloon angioplasty have been shown by several investigators [12,16]. However, these lasers have certain limitations: A shallow penetration depth of only 50 microns [19] necessitates direct contact with the atherosclerotic plaque, and because their medium is gas, they need alignment, calibration, and medium replenishment. Holmium:YAG lasers are pulsed-wave, solid-state lasers with a design that permits delivery of high peak powers with a short exposure time, achieving effective tissue ablation with little thermal damage to adjacent tissue [20]. Because the penetration depth of the holmium laser beam exceeds 400 microns, it provides effective ablation, even when the catheter tip is positioned at a distance from the target lesion [21]. The mid-infrared wavelength is highly absorbed by water, a major constituent of the atherosclerotic tissue, and it has the ability to ablate calcified tissue [22]. The holmium lasers are also unique in their compact size and ease of use, because they need no calibration or alignment. These characteristics have clinical advantages, especially when dealing with unstable patients needing urgent revascularization. Nevertheless, the cost and real clinical value of all wavelength lasers should be carefully considered nowadays in the new era of cost containment.

Thrombotic Lesions

The presence of intracoronary thrombus in unstable, ischemic coronary syndromes has been associated with an increased risk of complications during coronary balloon angioplasty [2]. Estella and coworkers [23] have demonstrated that success of the excimer laser is significantly compromised when thrombus is angiographically detected. In contrast, our study demonstrates that the presence of angiographically detected thrombus does not significantly increase the risk of poor clinical outcome and does not compromise the safety and efficacy of the holmium laser–assisted coronary angioplasty. These observations support the hypothesis that the holmium:YAG laser may have an important effect on thrombotic tissue in humans.

Role in Acute Myocardial Infarction

Mid-infrared laser, the wavelength of which coincides with strong water absorption peaks, seems appropriate for acute thrombolysis; a fresh thrombus is known to have a high water content, which results in a large thermal sink and, consequently, dissipation of laser thermal energy [24]. The utilization of this laser for both thrombolysis and plaque ablation [4,25] is warranted since only 14–38% of acute infarction patients qualify to receive thrombolytic drugs [26] and significant numbers of patients fail to benefit from these

agents. Furthermore, considering the need to achieve an open infarct-related artery for improved prognosis [27], mechanical revascularization is warranted for patients who are unsuitable candidates for thrombolytic agents, or who have clinically failed to respond to thrombolysis. Application of direct balloon angioplasty as the first line of therapy in acute myocardial infarction when the infarct-related artery contains large intracoronary thrombus and/or a complex lesion that is not ideal for balloon dilation is still controversial [28], because the immediate and short-term follow-up results include a 15% acute closure rate and an up to 60% restenosis rate within 6 months [28–30]. Investigators from the University of Miami were the first to utilize the holmium laser in acute myocardial infarction [31]. The finding in this series that 23 of the 24 patients with complicated acute myocardial infarction survived the infarction is encouraging. Thus, our initial clinical experience suggests that this technology can be safely applied in selected patients with acute myocardial infarction accompanied by ischemia and persistent angina.

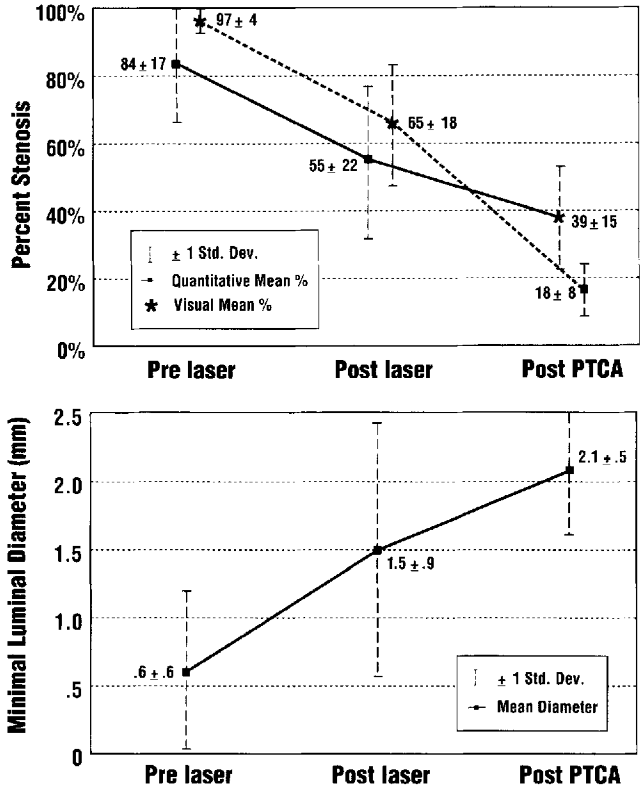


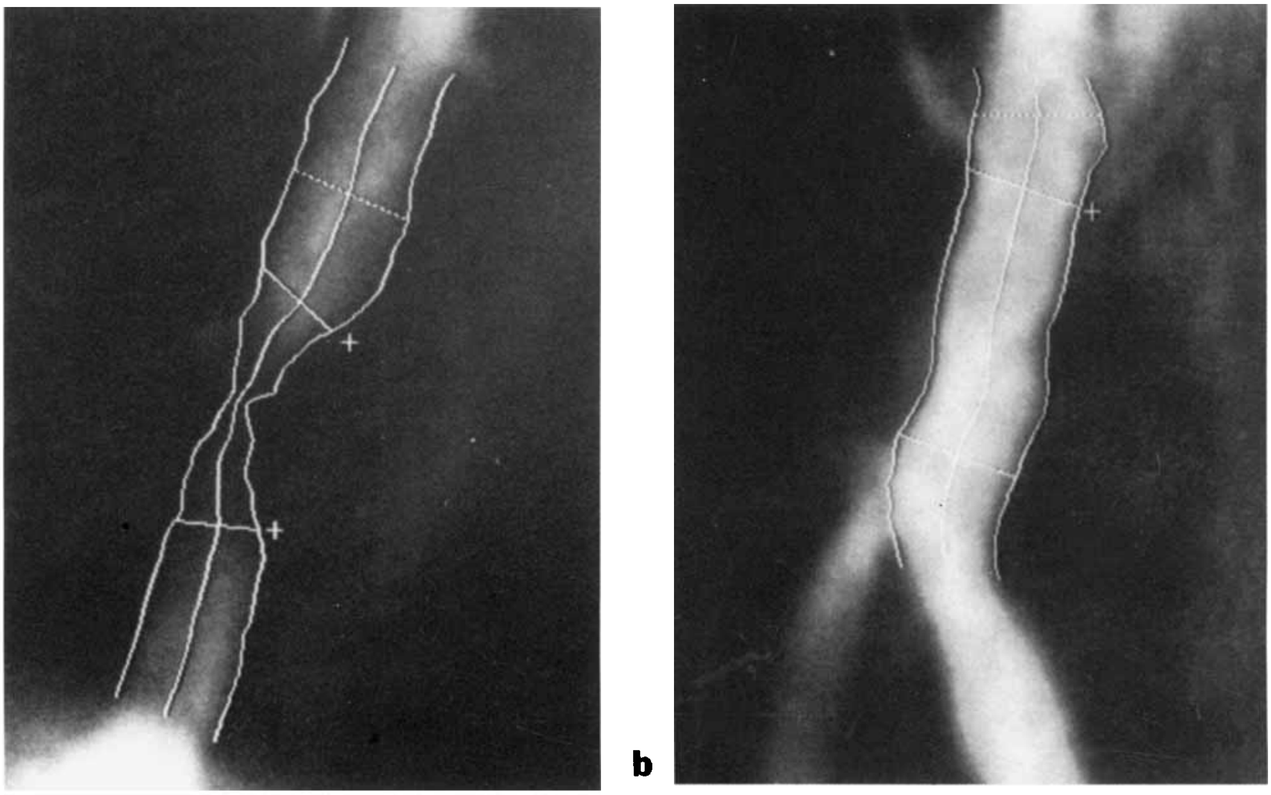
Fig. 3. Quantitative arteriographic analysis of percent diameter stenosis vs. visual estimation (**top**), and minimal luminal diameter (mm) (**bottom**) before (pre) and after (post) laser angioplasty (laser) and balloon angioplasty in 24 patients with acute myocardial infarction. Data are presented as mean ± SD.

Laser–Tissue Interaction

Experimental data show that the mid-infrared laser has a favorable laser–tissue interaction. By performing histologic studies on human and canine atherosclerotic arteries following holmium laser treatment, Kopchok and colleagues [32] identified effective tissue removal with a minimal zone of thermal effect to the intima and media confined to less than 20 microns. Isner [20] showed no thermal injury when holmium-induced ablation was carried out at a low fluence, similar to the fluence used in this study. Application of high fluences produced thermal injury. Likewise, Tomaru et al. [33] found that holmium:YAG could selectively ablate atheromatous tissue with minimal thermal injury. However, concern has been raised about "acoustic damage" in the form of fissures and dissections [19,34–36]. Clinically, our present experience does not support the latter observations. A possible explanation for the discrepancy between favorable clinical experience and unfavorable experimental results is that in those experiments lasing was carried out with a higher fluence than clinically recommended and was delivered through stiff, larger optic fibers [34] than those we have used.

Lasing Technique and Related Complications

Acute vessel closure, severe dissections, and perforations are among the most feared complications during laser angioplasty. Van Leeuwen et al. have shown that coronary dissections during excimer and mid-infrared laser angioplasty are caused by shock waves following a forceful vapor bubble expansion [37]. This effect seems to be prominent in blood and also seems to increase in the presence of calcified plaque. Recent studies indicate that the shock waves result in multiple layers of dissection, causing the arterial wall layers to "puff" up [38]. The phenomenon is termed *mille-feuilles,* because it resembles the many layers seen in the French pastry *mille-feuilles.* It results in acute vessel occlusion or flow-obstructing dissection. The effect cannot be relieved by nitrates and requires balloon angioplasty for effective remodeling of the disrupted layers. Of further concern is the production of heat during lasing. Significant heat generation can be measured in atherosclerotic plaques and their adjacent arte-



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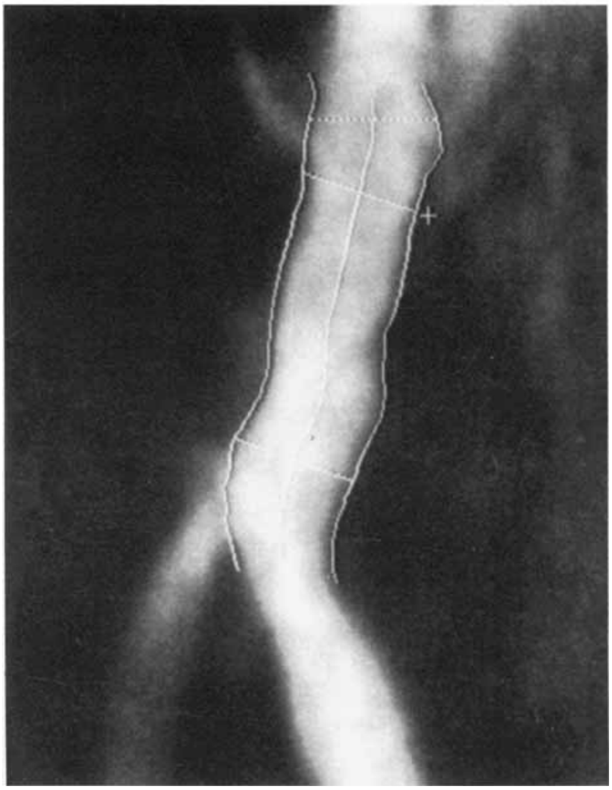

c

Fig. 4. **a:** Quantitative arteriographic measurement of an eccentric mid-right coronary artery stenosis (86% luminal narrowing). **b:** Post laser stenosis reduced to 45% following two passes of a 1.5 mm holmium laser catheter emitting 27 pulses. **c:** A residual stenosis (12%) of the same lesion after dilatation with a 2.5 mm balloon catheter.

rial wall, even with "cold," pulsed-wave lasers [39]. Heat is known to cause spasm of the coronary arterial wall [40].

The results of this study suggest the "pulse and retreat" lasing technique can reduce laser-associated complications. Conceivably, it eliminates wall injury because it allows time for the gas product to be swept away by forward coronary flow and enables cooling of the plaque and arterial wall between lasing sessions [8]. We are aware that early complications may represent an operator's learning curve, or may be unique to the holmium system in use. However, by utilizing the traditional lasing technique with an excimer laser, a significant incidence of vessel wall injury occurs, including a 2.6% perforation rate and a 18% dissection rate [16].

In summary, holmium:YAG laser angioplasty is safe and effective in patients with ischemic coronary artery disease who present with thrombus-containing lesions or nonthrombotic lesions. Importantly, the presence of intracoronary thrombus does not diminish the holmium laser procedural success rate. Similar to excimer laser angioplasty [16] and directional atherectomy [41], the effectiveness of the holmium laser in yielding long-term patency has not been proven. Con-

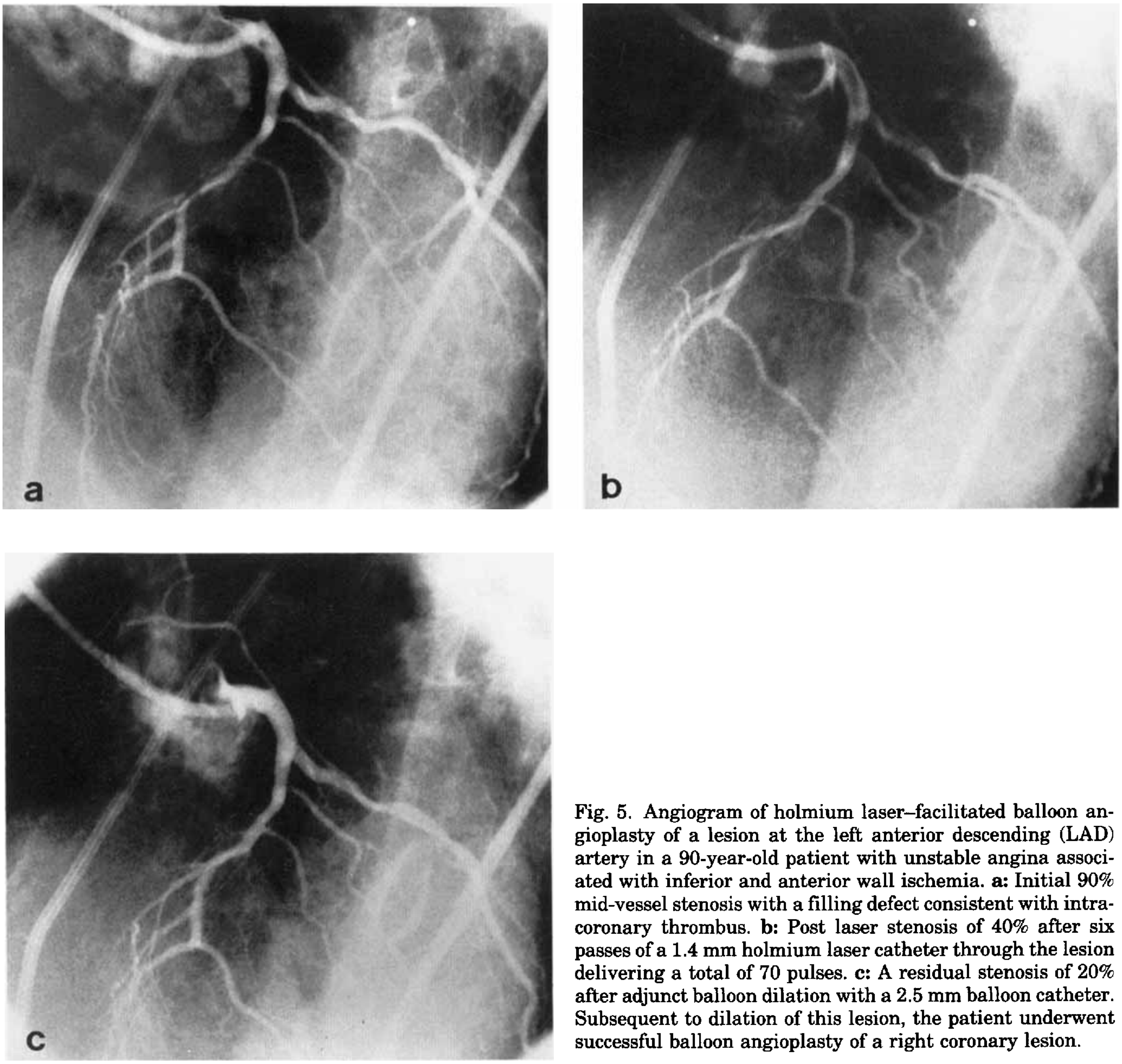

Fig. 5. Angiogram of holmium laser–facilitated balloon angioplasty of a lesion at the left anterior descending (LAD) artery in a 90-year-old patient with unstable angina associated with inferior and anterior wall ischemia. **a:** Initial 90% mid-vessel stenosis with a filling defect consistent with intracoronary thrombus. **b:** Post laser stenosis of 40% after six passes of a 1.4 mm holmium laser catheter through the lesion delivering a total of 70 pulses. **c:** A residual stenosis of 20% after adjunct balloon dilation with a 2.5 mm balloon catheter. Subsequent to dilation of this lesion, the patient underwent successful balloon angioplasty of a right coronary lesion.

trolled, randomized studies in larger series of patients are needed in order to further validate the clinical benefits of the holmium laser in acute coronary syndromes.

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